respectfully requested to consider these comments as well in his reconsideration of the outstanding rejection.

4. In conclusion

There is no prior art which suggests that Bi-clusters are suitable as primary ions in SIMS and there is no indication in the prior art that not only mass and charge state, but also its chemical properties, make Bi-clusters particularly suited primary ions in SIMS.

As explained above, none of the documents cited by the Examiner discloses or suggests the present invention. To the contrary, the Examiner combined four documents, not related to the present invention and even not related to each other, in an arbitrary manner, taking statements from these documents without regard to their actual meaning in their context.

For the reasons given above, this application is believed to be in condition for immediate allowance. A formal Notice of Allowance is accordingly respectfully solicited.

Respectfully submitted,

Karl F. Milde, Jr. Reg. No. 24,822

MILDE & HOFFBERG, LLP 10 Bank Street - Suite 460 White Plains, NY 10606

(914) 949-3100

I hereby certify that this correspondence is being deposited with the United States Postal Services as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

July 24, 2009 MILDE & HOFFBERG, LLP

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Date___July 24, 2009

Comments to the rejection of the United States Patent and Trademark Office

Application number 10/568,832

Hamza teaches an EBIT ion source producing slow and highly charged ions (HCI) for ultrasensitive surface analysis, e.g. Kr³³⁺, Xe⁴⁴⁺, Au⁶⁹⁺. The yields of secondary ions per incident ion are increased by two or three orders of magnitude compared to singly charged Xe ions, which allows a 10 to 100-fold improvement in sensitivity. The high potential energy of the HCI ions leads to a completely different sputtering and ionization process compared with lower charged primary ion species with high kinetic energy applied in conventional SIMS. The unusually high secondary ion yield permits the use of the powerful coincidence counting method.

Highly charged ions carry a large amount of **potential energy** (100 - 300 keV per incident ion) when they interact with a surface. Individual highly charged ions, such as Xe⁴⁴⁺ or Au⁶⁹⁺, deposit an unsually high density ... of electronic excitations onto a nanometer sized surface area in less than 10 femtoseconds. This extreme. localized excitation leads to **electronic sputtering** of the surface. (column 3, lines 28 - 37). In contrast, in conventional SIMS the high kinetic energy of several keV to some 10 keV is transferred by elastic collisions between the projectile and the target atoms in a so-called collision cascade (nuclear stopping). This mechanism of energy transfer is very different from the electronic excitation by highly charged ions.

The Bi cluster ion source according to the present invention emits primary ions species of the form $\mathrm{Bi_n}^{q^+}$ with charge state q and a number of n Bi atoms. Reasonable currents for SIMS measurements are only achieved with atomic and cluster ions of a charge state of q=1 to 3. For these species the potential energy of the multiply charged ions can be neglected and does not contribute to the sputtering and the ionization process.

Bi cluster ions of extremely high ionization states do not exist as they would directly undergo coulomb explosion.

It would be obvious for one of ordinary skill reading Hamza that the use of highly charged atomic ions with a potential energy of some 100 keV would be the key for an improvement of the sensitivity compared to the standard SIMS technique.

He would also conclude that

- 1. the mass and chemical nature of the projectile would not play any role but only the potential energy stored in highly charged ions (Xe⁴⁴⁺ or Au⁶⁹⁺).
- 2. liquid metal ion sources are not useful for high sensitivity as these sources do not provide ions with high charge states, and that an EBIT source producing highly charged ions is required.
- 3. cluster projectiles can not be used as these would undergo Coulomb explosion at high charge states.

Hence, all the teaching of Hamza leads completely away from the present invention.

Schultz improves a MALDI ionization process by implanting large metal clusters in biological tissues or organic solids. The implanted metal clusters are utilized as optical absorption sites for laser desorption and serve as a MALDI matrix. Analysis of the surface is performed by laser ablation and laser ionization. The disclosed analytical method does not use any mono or polyatomic primary ions for the <u>analysis</u> of the surface by SIMS.

Schultz investigates the use of primary ion clusters in order to prove advantages of very large cluster bombardment for the implantation process for MALDI. Primary ion species Au⁺, Au₃⁺, Au₅⁺, Au₉⁺, Au₉⁺, Au₉₀³⁺ are applied. Fig. 2 shows the effect of the implantation of Au on the MH⁺ ion yields of Gramicidin S. With an increasing number of gold atoms deposited per cm² the molecular ion yield decreases. Only for the very heavy Au₃₀₀³⁺ the ion yield of gramicidin S is stable even at high implantation. Although Fig. 2 shows an initial yield enhancement with the size of the Au cluster, the data presented by Schultz do not allow any estimate of the efficiency for metal cluster bombardment in SIMS as the consumption of sample material for the various projectiles is unknown.

Fig. 3 of Schultz et al. also indicates that irradiation with the large primary ion cluster Au₃₀₀³⁺ slightly enhances the molecular ion signal. Schultz states in Col. 6, line 35 - 38 "that the molecular ion signal is slightly enhanced after irradiation under the large cluster beam Au₃₀₀³⁺. Thus, a positive "matrix" effect from the shallow cluster implantation." Schultz teaches that the chemically derivatized implanted metal acts both as an optical absorption site and as a proton donor for forming MH⁺ peptide and protein ions and/or other biomolecular ions (Col. 6, line 49 - 52). In addition Schultz teaches that almost all the ions in the MALDI spectrum of Fig. 12 are the result of sodium or potassium attachment instead of the typical H⁺ attachment (Col. 12, line 17 - 19). The gold clusters could act as a matrix while the bombardment enhances impurity (alkali) incorporation (Col. 12, line 20 - 22).

In the Official Action Col. 12, line 19 - 21 of Schultz et al. is seen as proof that cluster bombardment significantly enhances the molecular ion yield. However, the corresponding statement of Schultz refers to a yield enhancement in MALDI, not in SIMS. The related spectrum in Fig. 12 is a MALDI spectrum, not a SIMS spectrum!

The use of Au for ion yield enhancement has a rather long history in the SIMS community.

A) Au and other noble metals have been used as a substrate for SIMS analysis of organic molecules for more than 30 years. The molecules are deposited as a monolayer on noble metal substrates. Benninghoven et al. (Benninghoven, Rüdenauer, Werner, Secondary Ion Mass Spectrometry, Basic Concepts, Instrumental Aspects, Applications and Trends, John Wiley & Sons, New York 1987, p. 750) published that as substrate the noble metals Au, Pt and Ag are particularly suited and show very high secondary ion yields (see Fig. 1). As an example the following figure shows the ion yield of the aminoacid Leucine for various metal substrate. The yield is normalized to the (M-H) yield for Au. The results clearly show that the chemistry of the metal is most important for the ion yield. Au shows the highest yield for (M+H) followed by Platinum Pt followed by Silver Ag. All other metals show ion yields that

are at least 3 orders of magnitude lower. This study shows that the chemical interaction between Au and the organic molecule Leucine is very favorable for positive and negative molecular ion formation. No data are given for Bi substrates. As a consequence of these results Au and Ag substrates have been used for SIMS in a large number of studies as substrate.



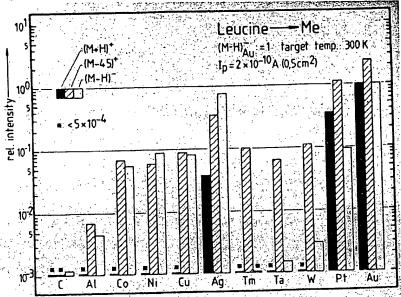


Fig. 5.36. Secondary ion emission from different substrates covered by a monolayer of leucine. From Lange et al. [863], with permission of the authors and North Holland Physics Publishing.

B) The very favorable influence of Au as substrate on the ion yields has also been used for bulk organic material. The deposition of Au onto the surface of organic materials leads to a strong increase of more than an order of magnitude although the surface is partially covered by Au (Delcorte et al., Analytical Chemistry 2002, 74, p. 4955). It has been observed that the deposition of Au onto the surface leads to the formation of cationized molecular ions with very high yields.

Therefore, the improvement of the ion yield and the matrix by the implantation of Au clusters close to the surface as proposed by Schultz is in agreement with these results.

The reader with ordinary skill would conclude that the chemical nature of Au has a particular advantage as a matrix for SIMS and for MALDI.

It would be obvious for one with ordinary skill reading Schultz that

- 1. it is very important to optimize the matrix for SIMS and MALDI by the implantation of Au cluster ions very close to the surface
- 2. that only very large gold clusters ions like Au_{300}^{3+} result in a slight enhancement (col. 6, line 45)
- 3. that the change of the chemistry close to the surface by implanted large Au clusters or alkali atoms is the dominant effect

In conclusion the teaching of Schultz would not give any indication for the advantage of using Bi clusters in SIMS. Schultz emphasizes the importance of the appropriate chemical matrix by Au implantation. However, it is not predictable in which way Bi cluster bombardment would alter the matrix and the chemistry. The completely different chemistry of Bi compared to Au could have a negative effect on the ion yield as well.

The Bi source does not provide very large clusters comparable to Au_{300}^{3+} that are considered by Schultz to be very important.

Moreover, Schultz does not give any indication that the mass of the atoms in the cluster is of importance and that a higher atomic mass per atom would be advantageous for the yield enhancement in SIMS.

Orloff discloses a liquid metal ion source with a three element asymmetric lens system providing a very low chromatic aberration. According to Orloff the chromatic aberration is limiting the minimum spot size obtainable (col. 1, lines 39-42) since ion beams produced by liquid metal field ionization sources have been found to have a high beam energy spread ΔE compared to other ion sources (col.1, lines 47-51). He teaches that in situations typical of lithography or surface analysis, high currents are desired in focused beam spots of approximately 1,000 - 2,000 Angstroms (column 1, lines 63-66). Orloff provides a method of operating an ion gun having a liquid metal field ionization source to provide reliable, uniform beam currents and to minimize energy spread of the ion beam produced by the ion gun (column 2, lines 28-32). He shows in Fig. 2A that for the optimized Gallium liquid metal ion source the energy spread at low emission currents would be about 5.3 eV.

It would be obvious for one of ordinary skill reading Orloff that it is extremely important for an intense and well focused beam to optimize a liquid metal ion source by selecting conditions to minimize the energy spread. For Gallium liquid metal ion guns the energy spread at optimum conditions would be as low as 5.3 eV.

Although Orloff shows exclusively data using a Gallium liquid metal ion gun based on a tungsten emitter, he states that "Similar experiments have also been performed with liquid Indium and liquid Bismuth, with results entirely analogous to those described above (column 10, lines 14-17). This statement can only refer to the properties of the physically asymmetric lens system and its focusing properties (co. 10, lines 10 - 14). The detailed performance characteristics like the energy spread at low emission currents are different for Ga and Bi.

Hence, Orloff does not give any indication that a Bi source would have any advantage over Ga and In in SIMS.

One of ordinary skill reading Hamza, Schultz and Orloff can easily check in the literature the factors that determine the energy spread of a liquid metal ion source. See for example Kim et.al. for the influence of the emitter temperature, (Kim et al., J. Phys. D: Appl. Phys. 31 (1998) 3463):

and G.L.R. Mair for the influence of the emission current and the mass (Mair, J.Phys.D:Appl.Phys. 29 (1996) 2186-2192):

$$\Delta E \propto I^{2/3} \ T^{1/2} \, m^{1/3}$$

Therefore, to minimize the energy spread the emission must be optimized for operation at

- low emission current I
- low temperature T of the liquid metal (see Orloff, Fig. 2a)
- low mass m of the ions.

The mass of Bi $(m=209\ u)$ as well as the melting temperature of Bi $(T=544\ K)$ are much higher than the corresponding values for Ga $(m=69\ u,\ T=303\ K)$. It is obvious for one of ordinary skill that Bi emitters have fundamental disadvantages over Ga emitters regarding the energy spread, which is cited by Orloff et al. as important (col. 2, l. 28).

No evidence is given by Orloff that using Bismuth would have any advantages over the Gallium emitters described. Orloff does not give any hint that a Bismuth liquid metal ion source would have any advantages in Secondary Ion Mass Spectrometry. In addition, Orloff does not give any hint that a Bi source would provide Bi clusters with high intensities and that the use of these clusters would have any advantage over the use of the atomic species.

Liebl discloses a method to improve the sensitivity in Secondary Ion Mass Spectrometry by bombarding the surface with chemically reactive ions. The preferred ions are those of elements that are highly electronegative, of relative large mass, and capable of forming strong chemisorptions bonds with the material under bombardment. (col.2, lines 19-22). Iodine ions are the preferred ions because of their relatively large mass and high reactivity (col. 2, lines 23-25). The described mechanism is based on a **strong chemical effect in SIMS**, the so-called matrix effect. It is well known that the secondary ion yields can vary several orders of magnitude depending on the <u>chemical environment</u> of the emitted species. Bombarding a surface with **highly electronegative ions** increases the work function of the bombarded surface and therefore **increases the ionization probability** of electropositive secondary ions. (col. 2, lines 45-59).

Fig. 7 summarizes the work of Liebl. It shows the relative yields of positive secondary aluminum ions from an aluminum target in response to bombardment by different primary ions. Fig. 7 proves that **the chemical effect is much more pronounced than the effect of the primary ions mass**. In contrast to the statement in the Official Action, the best results were not obtained with the highest mass projectile. Xe $(m=131 \ u)$ has the highest mass but compared to Iodine $(m=127 \ u)$ the secondary ion yield is about 2 orders of magnitude lower than the corresponding yield of Iodine. This clearly proves the chemical nature of the effect. A similar enhancement is obtained when changing from Ar $(m=40 \ u)$ to Cl $(m=35 \ u)$.

Bi $(m=209 \ u)$ has just a slightly higher mass of about 6 % compared to Au $(m=197 \ u)$. However the electronegativity of Bi of 1.9 is about 30 % lower than the electronegativity of Au of 2.4 (Handbook of Chemistry and Physics, 84th Edition, CRC Press, Boca Raton, Florida 2003, Section 9).

Reading Liebl one of ordinary skill would learn that the change of the chemistry by the implantation of electronegative primary ions would be most important for high ion yields. According to Liebl, there are no elements of maximum electronegativity available that have higher atomic mass than Iodine. In case Liebl would have considered heavy clusters as projectiles, he would have used Iodine clusters as clusters of atoms with highest electronegativity.

Hence, even if Liebl would have considered Bi and Au, he would not have used Bi instead of Au since the positive effect of the slightly higher mass of Bi compared to Au would be expected to be much lower than the negative effect of the lower electronegativity of Bi compared to Au.

In the Official Action it is stated that the empirical results of Liebl show that the secondary ion yield is directly proportional to the mass of the primary ion and is supported by a theory that secondary ion emission is equivalent to the yield of sputtered particles which increases with the atomic mass of the primary ions and their energies. This leads to the important consequence of the results of Liebl that the <u>efficiency</u> is <u>independent</u> of the mass of the primary ion. The higher mass leads to an increase of the ion yield and an equivalent increase of the sputter yield of the material. If a complete layer would be consumed by sputtering with electronegative projectiles of different mass, the total number of generated secondary ions would be constant and hence, the efficiency would be constant. Again, this shows, that the <u>chemistry</u> is most important to improve the efficiency for such sample systems studied by Liebl, not the mass of the primary ions. The higher mass of Bi would not lead to an increase in efficiency, but the higher electronegativity of the Au probably would.

Internal remark to the increase in mass of the atoms in a cluster (could be useful)

The examiner thinks that the increase in the atomic mass of the atoms of a cluster from Au to Bi is an obvious way to increase the yields and efficiencies. However, the general trend at the time of the invention was the use of clusters of lighter elements like C_{60} . This cluster has the light element C but a higher number of constituents. It has been reported that C_{60} gives significantly higher yields than Au_3 (see Fig. 2 below) (Weibel et al., Anal. Chem. 2003, 75, 1754 - 1764). It is also stated that the sample damage is significantly reduced for C60 which would correspond to a significant increase in the efficiency. The reader would conclude that it is better to use these projectiles instead of Au_3^+ . He would not conclude that the heavier Bi would have any advantages.

Figure 2

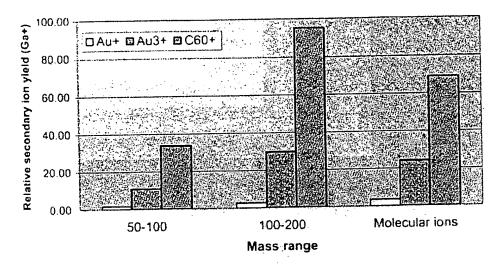


Figure 4. Comparison of positive secondary ion yields during analysis of PET using Au^+ , Au_3^+ , and C_{60}^+ primary ions at 10-keV impact energy.

General remarks to ion yields

It is well known in Secondary Ion Mass Spectrometry that the <u>chemistry</u> strongly influences the secondary ion yield. This effect is called the "matrix effect". The secondary ion yields of a particular element or molecule can vary over several orders of magnitude depending on the neighboring chemical species.

See for example J.C. Riviere, Handbook of surface and interface analysis, Marcel Dekker, New York 1998, p. 211:

"The number of sputtered ions per incident primary ion can also vary tremendously with the chemical environment in the near-surface layers, a phenomenon known as matrix effect. Examples of the secondray ion yield enhancement, which in some cases can reach several orders of magnitude, are described in".

See for example A. Benninghoven et al., Analytical Chemistry, Vol. 65, No. 14 (1993), page 632A:

"The charge state of sputtered particles depends largely on the chemical environment in the uppermost monolayer (matrix effect), which in general prevents the direct quantification of SIMS results."

General remarks to efficiency

In the literature most of the authors report on secondary ion yields and the changes of the yields by certain instrumental parameters like mass of the projectile, energy of the projectile, charge etc. However, a higher ion yield does not necessarily mean that the <u>efficiency</u> is increased as well.

The efficiency is determined by the ion yield per projectile and the sample consumption per projectile. The efficiency is increased if the ion yield is increased without increase of the sample consumption or if the ion yield is constant but the sample consumption per projectile is reduced.

Hamza and Schultz report about changes of the ion yield but do not give any information about the related change in sample consumption. Liebl shows that the increase in ion yield is proportional to the increase in sputter yield. Hence, the efficiency remains constant.

Conclusion:

- 1. One of ordinary skill would learn from Hamza,
 - to use highly charged ions with a high potential energy of 100 keV and more. The electronic sputtering by these highly charged ions improves the sensitivity by several orders of magnitude, compared to the conventional kinetic energy transfer of ions with a rather low number of charges.
 - to use an EBIT source that can produce such highly charged ions hence, he would be teached away from using Bi clusters with negligible potential energy and from using liquid metal ion sources to produce these Bi clusters with a very low number of charges.
- 2. One of ordinary skill would learn from Schultz,
 - that surface near implantation of very large Au clusters improves the ion yield by a favorable change of the chemistry and improves the matrix for formation of protonated or cationized molecular ions in SIMS and MALDI.
 - that only the use of the Au₃₀₀³⁺ results in a slight enhancement hence, he would be teached away from using metal clusters with a low number of atoms and he would be teached away from using other metals with different chemical properties than Au. He would not consider a Bi cluster source as it does not provide the very large clusters of the Au liquid metal ion source and has a completely different chemistry.

If one with ordinary skill reading Hamza and Schultz would do a search in the scientific literature, he would learn that Au is particularly suited as a substrate in contact with organic molecules and as a thin film by vapor deposition forming nanoclusters on organic surfaces. He would learn that Au is very popular in the SIMS community since decades. Even if he would consider Bi as an alternative to Au he would not get any hint from the SIMS literature that Bi would have comparable benefits for the ion formation.

The approaches of Hamza and Schultz are not compatible and lead into completely different directions (high potential energy by high number of charges for an atomic beam versus very large Au cluster beams with only a few charges).

- 3. One of ordinary skill would learn from Orloff,
 - that it is extremely important for intense, well focused beams from liquid metal ion sources to minimize the energy spread
 - that Ga has very favorable properties and that under optimum conditions the energy spread is 5.3 eV.
 - that similar experiments with asymetric lenses have also been performed with liquid Indium and liquid Bismuth (Col. 10, lines 10 17)

hence, reading Orloff he would not conclude that Bi sources have any advantage over the established Ga sources. He would not learn that a Bi liquid metal source emits Bi-clusters and that the use of these Bi clusters would be beneficial in SIMS.

If one with ordinary skill reading Orloff would do a search in the scientific literature about liquid metal ion sources, he would learn that the energy spread of Bi would be much larger than the energy spread of Ga due to the high mass and the high operating temperature. He would learn from Orloff that this source would be inferior to Ga.

Even if he would continue to consider Bi liquid metal ion sources, he would learn from Schultz that the chemistry change by the implantation of Au clusters is important and would understand that Bi has a completely different chemistry.

4. One of ordinary skill would learn from Liebl,

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- that the preferred primary ion species are highly electronegative, chemically reactive ions. The best results are consistently obtained with Iodine
- that elements with a lower electronegativity would have much poorer ion yields even if the mass is rather high (see Xe vs. I)
- that the efficiency is not improved by an increase of the mass of the projectile as the sputter yield and therefore, the sample consumption is increased by the same factor.

Learning from Schutz and Liebl that the chemical nature of the primary ion and the change of the matrix by the implantation is most important for the ionization, he would not have selected Bi. Instead he would see that Bi has a lower electronegativity than Au and would expect a poorer ion yield.

In conclusion the combination of the discussed publications teaches away from using Bi clusters as analysis species in SIMS. The different publications give completely different directions (high potential energy, very large Au clusters, liquid metal ion sources with very low energy spread, electronegative elements for improved ionisation in SIMS). There are no rules presented that can predict the efficiency to be expected for Bi clusters in SIMS compared to Au.

None of the publications teaches to use Bi in SIMS.

None of the publications teaches about the presence of Bi clusters in a Bi primary ion beam with good intensities.

None of these publications teaches about the use of Bi clusters in SIMS.

None of these publications teaches about the performance to be expected for Bi cluster beams (spot size, beam current ...) relative to Au liquid metal sources.